

REMARKS/ARGUMENTS

The undersigned attorney thanks Examiner Shawquia and SPE Rebecca Anderson the courtesy of the interview on July 7, 2009. The undersigned attorney pointed out that Hill et al. did not teach or suggest the used of reaction pressure {in step a)} other than room temperature, and did not teach or suggest the use of reaction pressure {in step a)} above room pressure, or at least above 5 bar, or of 5 to 10 bar. The undersigned attorney pointed that Hill et al., thereby directed one ordinary skilled in the art away from the claimed invention. Hill et al. disclosed primary amine reactants, but not secondary amine reactants. The Examiner had tried to use the secondary reference, Matsumoto, as teaching the reaction of secondary amines at elevated pressures. The undersigned attorney pointed that the chemistry of secondary amines was very different than the chemistry of primary amines (as had been pointed out in the previous amendment). The Examiner asserted that both references involved Mannich reactants. The undersigned attorney pointed that the yields using secondary amines is surprisingly much lower that when primary amines are used. One ordinary skilled in the art is directed away from the use of Matsumoto to change the invention/disclosure of Hill et al. The undersigned attorney asked about inserting the pressure range (5 to 10 bar) of Claim 37 into Claim 1. The SPE said that they would consider such amendment of Claim 1 and that such amendment probably would overcome the obviousness rejection.

[After the interview the undersigned attorney noted that dependent Claims 8 and 25 would be allowed if placed in independent form. Claims 8 and 25 were dependent (directly or indirectly) upon independent Claim 1. The reaction pressure of Claims 8 and 25 in reaction step a) is 5 to 10 bar. So the insertion of the reaction pressure {reaction step a)} of Claims 8 and 25 will make independent Claim 1 unobvious over the combination of Hill et al. and Matsumoto.]

Claims 1 to 7, 21 to 24 and 31 to 40 are pending. Claims 1, 31, 32 and 34 have been amended. Support for amending the pressure range in Claim 1 to "1.5 to 10 bar" is found in dependent Claims 8 and 25, which have been cancelled. Support for new Claim 40 is found in Example 7; new Claim 40 comes within the scope of the elected specie of Group II.

The Office Action stated: that Claims 1 to 8, 21 to 25 and 37 to 39 are currently pending in the instant application; that applicant has added new Claims 37 to 39 in the amendment filed on May 8, 2009; and that Claims 1, 3 to 7, 21 to 24, 33 and 39 are rejected; that Claims 2, 8, 25, 31 and 32 are objected to; and that Claims 34, 36, 37 and 38 are allowed in this Office Action.

The Office Action stated: that applicant's arguments, filed May 18, 2009, have overcome the rejection of Claims 2, 8, 25, 31, 34, and 35 under 35 USC 103 as being unpatentable over Hill et al in View of Matsumoto; and that the above rejection has been withdrawn relating to the indicated claims.

Dependent Claims 2, 8, 25, 31 and 32 have also objected to as being dependent upon a rejected based claim. Applicant traverses this objection.

The Office Action stated that, to overcome this objection, applicant should rewrite said claims in an independent form and include the limitations of the base claim and any intervening claim. Applicant has amended independent Claim 1 to recite the content of Claims 8 and 25 (now cancelled), that are drawn to the pressure during step a) being in the range of 1.5 to 10 bar. The Examiners, during the interview, stated that insertion of this limitation would probably overcome the Section 103(a) rejection of independent Claim 1 (which meant also the dependent claims thereof).

The Office Action stated that following is a quotation of 35 U.S.C. § 103(a) that forms the basis for the obviousness rejection set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3 to 7, 21 to 24, 33, 35 and 39 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Hill et al. in view of Matsumoto. Applicant traverses this rejection.

Independent Claim 1 (and its dependent claims) are allowable over the combination of Hill et al. and

Matsunoto since the pressure range in step a) of allowable dependent Claims 8 and 25 have been inserted into independent Claim 1.

Nowhere does Hill et al. disclose the pressure being used when the primary amine is involved in reaction, hence, in the usage in science and technology, the temperature and pressure used is standard room temperature and standard (sea level) atmospheric pressure (STP). There is no teaching or suggestion in Hill et al. that the reaction pressure used was above standard (sea level) atmospheric pressure. The burden of proof is upon the Examiner and she has not carried her burden of proof.

Hill et al. uses primary amines in its reaction scheme but does not teach or suggest the use of any elevated reaction pressure [even in the original (prior) synthesis scheme it discloses on page 812]. Applicant's claimed invention as whole, that uses elevated reaction pressure, and the unexpected and surprising results and advantages thereof, are clearly not taught or suggested by Hill et al. to one ordinarily skilled in the art.

The Examiner has attempted to correct the defects of Hill et al. in the search for applicant's claimed invention by combining Matsumoto with et al., but the attempt fails. Matsumoto only uses secondary amines. As all of the prior art teaching have to be considered under Section 103(a), there is no reason of record not to replace the primary amine of Hill et al. with the secondary amine of Matsumoto. Hence, the combination would result in use of a secondary amine at standard (sea level) atmospheric pressure – Matsumoto results in direction away from applicant's claimed invention. The use of a secondary amine without pressure is not too bad – another direction away from applicant's claimed invention.

The main difference from applicant's process compared to Matsumoto is that applicant reacts primary amines at a pressure of 1.5 to 10 bar. Applicant's claimed invention provides surprising and unexpected results. A secondary amine with a formaldehyde source and a ketone gives a tertiary amine, eventually at low yields. A primary amine with a formaldehyde source and a ketone normally gives, if at all, a secondary amine at a very low yield, and a branched tertiary amine, wherein the primary amine is added twice to the formaldehyde source and a ketone, normally at low yields. In some cases

said tertiary amine can be split up into the corresponding secondary amine product of applicant's invention process. But such result is not sure for every compound and furthermore also reduces the yield – plus such process has another/further step that add desirable expense, time, etc. If Matsumoto is used, applicant's invention is clearly unobvious over the combination of rejection references.

The different chemistry between primary and secondary references and the cataclysmic effect to the products shows why, among other reasons, one ordinarily skilled in the art would not use Matsumoto in an obviousness rejection of applicant's claimed process.

The differences between applicant's Claim 1 and the disclosure of Hill et al. (even when Matsumoto is attempted to be added) is inventive, patentable and unexpected over Hill et al. Applicant's Claim 1 primarily differs from Hill et al. by working under a pressure of 1.5 to 10 bar. This difference in pressure surprisingly is sufficient to achieve a complete change in product composition from Hill et al.

Hill et al prepared tritium labeled compounds according to known methods. According to the literature Hill et al. expected (page 813, fourth and fifth paragraphs) and obtained only low yields. In some experiments with derivatized starting compounds it was not possible even to separate the desired secondary Mannich base (secondary amine) from the reaction mixture. If the present process would have been obvious to the person skilled in the art, Hill et al. clearly would have applied modest pressure to obtain remarkably higher yields. This applies especially in a case where highly dangerous and expensive radioactive labeled compounds have to be handled.

It should be noted that starting from compounds where R^2 is an optionally substituted alkyl residue, the reaction without pressure gives only a small amount of the desired product. Sometimes no secondary base can be isolated at all. For such starting compounds the tertiary amine of formula III is the main product of the reaction below atmospheric pressure.

In the literature (Mannich et al., 1922, Blicke et al., 1942, and Becker, 1969, all documents cited in the application) it has been demonstrated that unless R^2 is a bulky residue formation of the tertiary base (tertiary amine) prevails by far over the formation of the secondary Mannich base (secondary amine). Decomposition of the tertiary amine of formula III can occur to form the secondary amine in poor

yield by applying, for example, steam distillation while the major part of the product forms a brown to black sticky pitch-like mixture.

Applying pressure according to applicant's patentable process almost completely avoids formation of the tertiary amine and yields the secondary amine almost free of decomposition by-products regardless which residue R² is attached to the amine source. Hill et al. is not even suggestive of this unexpected result – nor is Matsumoto by itself or in attempted combination with Hill et al.

Thus, applying pressure above atmospheric pressure does not only improve the yield but also makes it possible to directly obtain any desired tertiary amine. This is patentable over Hill et al. (even when Matsumoto's process using secondary amines is added, or attempted to be added).

Hill et al. in view of Matsumoto does not provide any (strong, weak or otherwise) showing of prima facie obviousness and does not result applicant's claimed invention. Applicant has shown that one ordinarily skilled in the art would not combine Hill et al. and Matsumoto in the search for applicant's claimed invention. Hill et al. makes the claimed invention unobvious to one ordinarily skilled in the art, and Matsumoto does not cure the defects of Hill et al. in the search for applicant's claimed invention. Matsumoto directs one ordinarily skilled in the art away from applicant's claimed invention.

There is no resolution of the level of ordinary skill in the record (as required by the Supreme Court, Patent Office policy and the patent statute), there cannot be a valid rejection of obviousness under 103(a). There cannot be a prima facie showing of obviousness, because there cannot be a valid rejection of obviousness under Section 103(a) in the present case as there is no resolution of the level of ordinary skill in the art in the record.

In trying to establish a case of prima facie obviousness, the Office Action also has the heading "The Scope and Content of the Prior Art (MPEP §2141.01)". The attempt to factually establish a showing prima facie obviousness fails for the above reasons.

In trying (unsuccessfully) to establish a case of prima facie obviousness, the Office Action further had the heading "The Difference Between the Prior Art and the Claims (MPEP §2141.02)". The different results obtained by the difference in

reaction pressure is unexpected and shows the unobviousness of the claimed invention.

In trying (unsuccessfully) to establish a case of prima facie obviousness, the Office Action also had the heading "Prima Facie Obviousness – The Rational and Motivation (MPEP §2142-2143)". The unexpected results of applicant's claimed invention show that no prima facie showing of obviousness has ever existed or been established.

Applicant requests that this rejection be withdrawn.

Reconsideration, reexamination and allowance of the claims are respectfully requested.

March 1, 2010
Date

Virgil H. Marsh
Virgil H. Marsh
Reg. No. 23, 083

Fisher, Christen & Sabol
Suite 603
1156 Fifteenth Street, N.W.
Washington, D.C. 20005
Tel.: 202 659-2000
Fax: 202) 659-2015

<p align="center">+CERTIFICATE OF MAILING</p> <p>I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on <u>March 1, 2010.</u></p> <p align="center"><u>Virgil H. Marsh</u> FISHER, CHRISTEN & SABOL 1156 15th St., NW, Suite 603 Washington, D.C. 20005</p>
